

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-75(cancelled)

76. (new) A method for modulating the immune response of a subject, the method comprises administering to said subject a sphingoid-polyalkylamine conjugate together with a biologically active molecule, the biologically active molecule being effective to modulate said immune response.

77. (new) The method of Claim 76, wherein said sphingoid-polyalkylamine conjugate comprises a sphingoid backbone carrying, via a carbamoyl bond at least one polyalkylamine chain.

78. (new) The method of Claim 76, wherein said modulation includes stimulation or enhancement of the immune response.

79. (new) The method of any one of Claims 76, wherein said biologically active molecule is associated with said sphingoid-polyalkylamine conjugate.

80. (new) The method of Claim 76, wherein said biologically active molecule has, at a physiological pH, a net negative dipole moment, a net negative charge or contains at least one region having a net negative charge.

81. (new) The method of Claim 76, wherein said biologically active molecule is an immunomodulator selected from a nucleic acid molecule, an amino acid molecule or a low molecular weight compound.

82. (new) The method Claim 76, wherein said biologically active molecule is selected from an antigenic protein, antigenic peptide, antigenic polypeptide, or a carbohydrate.

83. (new) The method Claim 76, wherein said nucleic acid molecule is an oligodeoxynucleotides (ODN).

84. (new) The method of Claim 76, further comprising administering to said subject an immunostimulating agent.

85. (new) The method of Claim 84, wherein said immunostimulating agent is administered concomitant with, or within a time interval before after administration of said sphingoid-polyalkylamine conjugate.

86. (new) The method of Claim 76, wherein said sphingoid-polyalkylamine conjugate forms a lipid assembly.

87. (new) The method of Claim 86, wherein said lipid assembly comprises vesicles or micelles or combination of same.

88. (new) The method of Claim 87, wherein said biologically active molecule is associated with said lipid assembly.

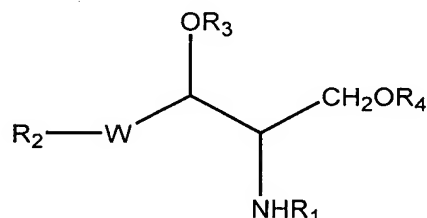
89. (new) The method of Claim 76, wherein the sphingoid is selected from ceramide, dihydroceramide, phytoceramide, dihydrophytoceramide, ceramine, dihydroceramine, phytoceramine, dihydrophytoceramine.

90. (new) The method of Claim 89, wherein said sphingoid is ceramide.

91. (new) The method of Claim 90, wherein said polyalkylamine is selected from spermine, spermidine, a polyamine analog or a combination of same thereof.

92. (new) The method of Claim 76, wherein said sphingoid-polyalkylamine conjugate is N-palmitoyl D-erythro sphingosyl carbamoyl-spermine (CCS).

93. (new) The method of Claim 76, wherein said sphingoid-polyalkylamine conjugate has the following formula (I):



wherein

R₁ represents a hydrogen, a branched or linear alkyl, aryl, alkylamine, or a group -C(O)R₅;

R₂ and R₅ represent, independently, a branched or linear C₁₀-C₂₄ alkyl, alkenyl or polyenyl groups;

R₃ and R₄ are independently a group -C(O)-NR₆ R₇, R₆ and R₇ being the same or different for R₃ and R₄ and represent, independently, a hydrogen, or a saturated or unsaturated branched or linear polyalkylamine, wherein one or more amine units in said

polyalkylamine may be a quaternary ammonium; or R_3 is a hydrogen; or

R_3 and R_4 form together with the oxygen atoms to which they are bound a heterocyclic ring comprising $-C(O)-NR_9-[R_8-NR_9]_m-C(O)-$, R_8 represents a saturated or unsaturated C_1-C_4 alkyl and R_9 represents a hydrogen or a polyalkylamine of the formula $-[R_8-NR_9]_n-$, wherein said R_9 or each alkylamine unit R_8NR_9 may be the same or different in said polyalkylamine; and

n and m , represent independently an integer from 1 to 10;

W represents a group selected from $-CH=CH-$, $-CH_2-CH(OH)-$ or $-CH_2-CH_2-$.

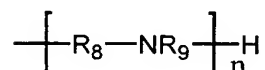
94. (new) The method of Claim 93, wherein R_1 represents a $-C(O)R_5$ group, R_5 being as defined.

95. (new) The method of Claim 93, wherein said R_2 and R_5 represent, independently, a linear or branched $C_{12}-C_{18}$ alkyl or alkenyl groups.

96. (new) The method of Claim 93, wherein W represents $-CH=CH-$.

97. (new) The method of Claim 93, wherein R_1 represents a $-C(O)R_5$ group; R_5 represents a $C_{12}-C_{18}$ linear or branched alkyl or

alkenyl; **W** represents $-\text{CH}=\text{CH}-$; **R₂** represents a C₁₂-C₁₈ linear or branched alkyl or alkenyl; **R₃** and **R₄** represent, independently, a group $\text{C}(\text{O})-\text{NR}_6\text{R}_7$, and **R₃** may also represent a hydrogen, wherein **R₆** and **R₇** represent, independently, a hydrogen or a polyalkylamine having the general formula (II):



wherein

R₈ represent a C₁-C₄ alkyl;

R₉ represents a hydrogen or a polyalkylamine branch of formula (II), said **R₈** and **R₉** may be the same or different for each alkylamine unit, $-\text{R}_8\text{NR}_9-$, in the polyalkylamine of formula (II); and

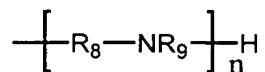
n represents an integer from 3 to 6.

98. (new) The method of Claim 93, wherein **R₃** is a hydrogen atom.

99. (new) The method of Claim 93, wherein both **R₃** and **R₄** represent the same or a different polyalkylamine.

100. (new) The method of Claim 93, wherein **R₁** represents a $-\text{C}(\text{O})\text{R}_5$ group; **R₅** represents a C₁₂-C₁₈ linear or branched alkyl or alkenyl; **W** represents $-\text{CH}=\text{CH}-$; **R₂** represents a C₁₂-C₁₈ linear or branched alkyl or alkenyl; **R₃** and **R₄** represent independently a

group C(O)-NR₆R₇, wherein **R₆** and **R₇** represent, independently, an alkylamine or a polyalkylamine having the general formula (II):



wherein

R₈ represent a C₁-C₄ alkyl;

R₉ represents a hydrogen or a polyalkylamine branch of formula (II), said **R₈** and **R₉** may be the same or different for each alkylamine unit, -**R₈****NR₉**-, in the polyalkylamine of formula (II); and

n represents an integer from 3 to 6.

101. (new) The method of Claim 93, wherein **R₁** represents a C(O)**R₅** group; **R₅** represents a C₁₂-C₁₈ linear or branched alkyl or alkenyl; **W** represents -CH=CH-; **R₂** represents a C₁₂-C₁₈ linear or branched alkyl or alkenyl; **R₃** and **R₄** form together with the oxygen atoms to which they are bonded a heterocyclic ring comprising -C(O)-[NH-**R₈**]_{**n**}-NH-C(O)-,

wherein

R₈ represents a C₁-C₄ alkyl, wherein for each alkylamine unit having the formula -NH-**R₈**-, said **R₈** may be the same or different; and **n** represents an integer from 3 to 6.

102. (new) The method of Claim 93, wherein said **R₈** is a C₃-C₄ alkyl.

103. (new) The method of Claim 76, wherein said biologically active material is derived from influenza virus or an analog of a molecule derived from influenza virus.

104. (new) The method of Claim 103, wherein said biologically active material is a combination of hemagglutinin and neuraminidase (HN).

105. (new) The method of Claim 76, comprising intranasal or intramuscular administration of said conjugate.

106. (new) The method of Claim 92, comprising intranasal or intramuscular administration of said N-palmitoyl D-erythro sphingosyl carbamoyl-spermine together with said biologically active molecule.

107. (new) A method for stimulating or enhancing the immune response of a subject to influenza virus, the method comprises providing said subject with N-palmitoyl D-erythro sphingosyl carbamoyl-spermine (CCS) together with an influenza antigen.

108. (new) A vaccine comprising sphingoid-polyalkylamine conjugate and an amount of a biologically active molecule, the amount of said biologically active molecule being effective to modulate the immune response of a subject.

109. (new) The vaccine of Claim 108, wherein said biologically active molecule is effective to stimulate or enhance the immune response of said subject.

110. (new) The vaccine of Claim 109, further comprising an immunostimulating agent.

111. (new) The vaccine of claim 108, wherein said sphingoid-polyalkylamine conjugate comprises a sphingoid backbone carrying, via a carbamoyl bond at lest one polyalkylamine chain.

112. (new) The vaccine of Claim 111, wherein said sphingoid backbone is selected from ceramide, dihydroceramide, phytoceramide, dihydrophytoceramide, ceramine, dihydroceramine, phytoceramine, dihydrophytoceramine.

113. (new) The vaccine of Claim 112, wherein said sphingoid is ceramide.

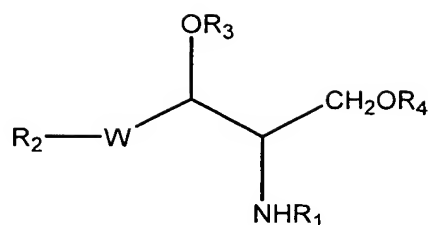
114. (new) The vaccine of Claim 108, wherein said polyalkylamine chain is selected from spermine, spermidine or a polyalkylamine analog of spermine or spermidine.

115. (new) The vaccine of Claim 108, wherein said sphingoid-polyalkylamine conjugate is N-palmitoyl D-erythro sphingosyl carbamoyl-spermine (CCS).

116. (new) The vaccine of Claim 115, wherein said biologically active molecule is a molecule derived from influenza virus or is an analog of a molecule derived from influenza virus.

117. (new) A vaccine comprising N-palmitoyl D-erythro sphingosyl carbamoyl-spermine (CCS) in combination with hemagglutinin neuraminidase.

118. (new) The vaccine of Claim 108, wherein said sphingoid-polyalkylamine conjugate has the following formula (I):



wherein

R₁ represents a hydrogen, a branched or linear alkyl, aryl, alkylamine, or a group -C(O)R₅;

R₂ and **R₅** represent, independently, a branched or linear C₁₀-C₂₄ alkyl, alkenyl or polyenyl groups;

R₃ and **R₄** are independently a group -C(O)-NR₆ R₇, **R₆** and **R₇** being the same or different for R₃ and R₄ and represent, independently, a hydrogen, or a saturated or unsaturated branched or linear polyalkylamine, wherein one or more amine units in said polyalkylamine may be a quaternary ammonium; or **R₃** is a hydrogen; or

R₃ and **R₄** form together with the oxygen atoms to which they are bound a heterocyclic ring comprising -C(O)-NR₉-[R₈-NR₉]_m-C(O)-, **R₈** represents a saturated or unsaturated C₁-C₄ alkyl and **R₉** represents a hydrogen or a polyalkylamine of the formula -[R₈-NR₉]_n-, wherein said R₉ or each alkylamine unit R₈NR₉ may be the same or different in said polyalkylamine; and

n and **m**, represent independently an integer from 1 to 10;

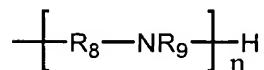
W represents a group selected from $-\text{CH}=\text{CH}-$, $-\text{CH}_2-\text{CH}(\text{OH})-$ or $-\text{CH}_2-\text{CH}_2-$.

119. (new) The vaccine of Claim 118, wherein R_1 represents a $-\text{C}(\text{O})\text{R}_5$ group, R_5 being as defined.

120. (new) The vaccine of Claim 118, wherein said R_2 and R_5 represent, independently, a linear or branched $\text{C}_{12}-\text{C}_{18}$ alkyl or alkenyl groups.

121. (new) The vaccine of Claim 118, wherein **W** represents $-\text{CH}=\text{CH}-$.

122. (new) The vaccine of Claim 118, wherein R_1 represents a $-\text{C}(\text{O})\text{R}_5$ group; R_5 represents a $\text{C}_{12}-\text{C}_{18}$ linear or branched alkyl or alkenyl; **W** represents $-\text{CH}=\text{CH}-$; R_2 represents a $\text{C}_{12}-\text{C}_{18}$ linear or branched alkyl or alkenyl; R_3 and R_4 represent, independently, a group $\text{C}(\text{O})-\text{NR}_6\text{R}_7$, and R_3 may also represent a hydrogen, wherein R_6 and R_7 represent, independently, a hydrogen or a polyalkylamine having the general formula (II):



wherein

R_8 represent a C_1-C_4 alkyl;

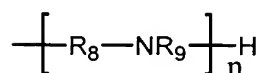
R₉ represents a hydrogen or a polyalkylamine branch of formula (II), said **R₈** and **R₉** may be the same or different for each alkylamine unit, **-R₈NR₉-**, in the polyalkylamine of formula (II); and

n represents an integer from 3 to 6.

123. (new) The vaccine of Claim 118, wherein **R₃** is a hydrogen atom.

124. (new) The vaccine of Claim 118, wherein both **R₃** and **R₄** represent the same or a different polyalkylamine.

125. (new) The vaccine of Claim 118, wherein **R₁** represents a **-C(O)R₅** group; **R₅** represents a **C₁₂-C₁₈** linear or branched alkyl or alkenyl; **W** represents **-CH=CH-**; **R₂** represents a **C₁₂-C₁₈** linear or branched alkyl or alkenyl; **R₃** and **R₄** represent independently a group **C(O)-NR₆R₇**, wherein **R₆** and **R₇** represent, independently, an alkylamine or a polyalkylamine having the general formula (II):



wherein

R₈ represent a **C₁-C₄** alkyl;

R₉ represents a hydrogen or a polyalkylamine branch of formula (II), said **R₈** and **R₉** may be the same or different for each

alkylamine unit, $-R_8NR_9-$, in the polyalkylamine of formula (II);
and

n represents an integer from 3 to 6.

126. (new) The vaccine of Claim 118, wherein R_1 represents a $C(O)R_5$ group; R_5 represents a $C_{12}-C_{18}$ linear or branched alkyl or alkenyl; W represents $-CH=CH-$; R_2 represents a $C_{12}-C_{18}$ linear or branched alkyl or alkenyl; R_3 and R_4 form together with the oxygen atoms to which they are bonded a heterocyclic ring comprising $-C(O)-[NH-R_8]_n-NH-C(O)-$,

wherein

R_8 represents a C_1-C_4 alkyl, wherein for each alkylamine unit having the formula $-NH-R_8-$, said R_8 may be the same or different; and n represents an integer from 3 to 6.

127. (new) The vaccine of Claim 118, wherein said R_8 is a C_3-C_4 alkyl.

128. (new) A kit comprising a sphingoid-polyalkylamine and instructions for use of said sphingoid-polyalkylamine conjugate in combination with a biologically active molecule for the preparation of a vaccine, the biologically active molecule capable of modulating an immune response in a subject.

129. (new) The kit of Claim 128, wherein said sphingoid-polyalkylamine conjugate is N-palmitoyl D-erythro sphingosyl carbamoyl spermine (CCS).

130. (new) The kit of Claim 129, for the preparation of an influenza vaccine.

131. (new) A complex comprising a sphingoid-polyalkylamine conjugate and a biologically active molecule capable of modulating an immune response of a subject.

132. (new) The complex of Claim 131 comprising N-palmitoyl D-erythro sphingosyl carbamoyl spermine (CCS) associated with said biologically active molecule.

133. (new) The complex of Claim 132, wherein said complex comprises a lipid assembly, the lipid assembly comprising N-palmitoyl D-erythro sphingosyl carbamoyl spermine (CCS) associated with said biologically active molecule.

134. (new) The complex of Claim 133, wherein said lipid assembly is a liposome, a vesicle or a combination of same.